```
### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 3106900061...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS?tkq0ljkh ********
Welcome to DIALOG
### Status: Connected


Dialog level 00.12.12D

Last logoff:  09jan01 11:24:51
Logon file405 13feb01 07:21:53
           ***ANNOUNCEMENT ***
                  ***
NEW FILE RELEASED
***Investext PDF Index (File 745)
***Daily and Sunday Telegraph (London) Papers (File 756)
***The Mirror Group Publications (United Kingdom) (File 757)

UPDATING RESUMED
***Extel News Cards from Primark (File 501)
***TFSD Ownership Database (File 540)
                          ***
RELOADED
***Kompass Asia/Pacific (File 592)
***Kompass Central/Eastern Europe (File 593)
***Kompass Latin America (File 586)
***Brands and their Companies (File 116)
***Kompass USA (File 584)
***Kompass Canada (File 594)
***PsycINFO (File 11)
FILES REMOVED
***EconBase (File 565)
***Unlisted Drugs (File 140)

>>>Get immediate news with Dialog's First Release
   news service.  First Release updates major newswire
   databases within 15 minutes of transmission over the
   wire.  First Release provides full Dialog searchability
   and full-text features.  To search First Release files in
   OneSearch simply BEGIN FIRST for coverage from Dialog's
   broad spectrum of news wires.

     >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
     >>>    of new databases, price changes, etc.      <<<
                  ****
KWIC is set to 50.
HILIGHT set on as '*'
PICKS is set ON as an alias for 5,55,159,143,358,340,344,348,351,352,447,72,73,154,1
55,349.
*** NEW Current Year Ranges Install ***
SYSTEM:HOME
Menu System II: D2 version 1.7.8 term=ASCII
                     *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
```

3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:
6. DIALOG(R) Document Delivery
7. Data Star(R)

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).
?b picks

>>> 351 is unauthorized
>>> 352 is unauthorized
>>>2 of the specified files are not available
13feb01 07:22:18 User243038 Session D55.1
$0.00 0.220 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.02 TYMNET
$0.02 Estimated cost this search
$0.02 Estimated total session cost 0.220 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2001/Feb W1
(c) 2001 BIOSIS
File 55:Biosis Previews(R) 1993-2001/Feb W1
(c) 2001 BIOSIS
File 159:Cancerlit 1975-2000/Nov
(c) format only 2000 Dialog Corporation
***File 159: For changes to the file please see Help News159.**
File 143:Biol. & Agric. Index 1983-2001/Dec
(c) 2001 The HW Wilson Co
File 358:Current BioTech Abs 1983-1999/Dec
(c) 1999 DECHEMA
***File 358: Updates delayed. Please see HELP NEWS 358 for details.**
File 340:CLAIMS(R)/US PATENT 1950-01/JAN 30
(c) 2001 IFI/CLAIMS(R)
***File 340: Price changes as Of 1/1/01. Please see HELP RATES 340.**
File 344:CHINESE PATENTS ABS APR 1985-2001/JAN
(c) 2001 EUROPEAN PATENT OFFICE
File 348:EUROPEAN PATENTS 1978-2000/Jan W05
(c) 2001 European Patent Office
File 447:IMSWorld Patents International 2001/Jan
(c) 2001 IMSWorld Publ. Ltd.
File 72:EMBASE 1993-2001/Feb W1
(c) 2001 Elsevier Science B.V.
***File 72: For information about Explode feature please**
see Help News72.
File 73:EMBASE 1974-2001/Feb W1
(c) 2001 Elsevier Science B.V.
***File 73: For information about Explode feature please**
see Help News73.
File 154:MEDLINE(R) 1993-2000/Dec W4
(c) format only 2000 Dialog Corporation
***File 154: First Medline 2001 update is expected towards the end of**
February. For other NLM information see Help News154.
File 155:MEDLINE(R) 1966-2000/Dec W4
(c) format only 2000 Dialog Corporation
***File 155: First Medline 2001 update is expected towards the end of**
February. For other NLM information see Help News155.

File 349:PCT Fulltext [redacted]3-2001/UB=20010208, UT=2001012[redacted]
(c) 2001 WIPO/Mi[redacted]Pat
***File 349: Phase 2 enhancements with current WIPO biblio data now online.**
See HELP NEWS 349 for more information.

Set	Items	Description

?e au=schneider, r j

Ref	Items	Index-term
E1	1	AU=SCHNEIDER, PETER M
E2	3	AU=SCHNEIDER, R
E3	0	*AU=SCHNEIDER, R J
E4	13	AU=SCHNEIDER, R.
E5	1	AU=SCHNEIDER, R. C
E6	2	AU=SCHNEIDER, R. E
E7	1	AU=SCHNEIDER, R. J.
E8	4	AU=SCHNEIDER, R. K
E9	1	AU=SCHNEIDER, R. M
E10	1	AU=SCHNEIDER, R. P
E11	1	AU=SCHNEIDER, R. P.
E12	17	AU=SCHNEIDER, R. W

Enter P or PAGE for more
?t e7
>>>No sets currently exist
?s e7
>>>One or more prefixes are unsupported
>>> or undefined in one or more files.
S1 1 AU="SCHNEIDER, R. J."
?d s1
Display 1/2/1 (Item 1 from file: 358)
DIALOG(R)File 358:Current BioTech Abs
(c) 1999 DECHEMA . All rts. reserv.

083701 CBA Acc. No.: 14-08-006730 DOC. TYPE: Patent
Amplified hybridization assay.
AUTHOR: *Schneider, R. J. *; Shenk, T. E.
CODEN: USXXAM
PATENT NUMBER: US 5424188
PATENT APPLICATION: US 963923 (921020)
COMPANY: Princeton Univ. , Princeton, NJ , USA </>
PUBLICATION DATE: 13 Jun 1995 (950613) / (19950613) LANGUAGE: English
DESCRIPTORS: diagnostic kit ; hybridization ; assay ; nucleic acids ; DNA probes ; gene probe
SECTION: Genetic Manipulation (03)

- end of display -
?e au= jamal, sumayah

Ref	Items	Index-term
E1	1	AU=JAMAL, S. ARSHAD
E2	2	AU=JAMAL, SAJID
E3	0	*AU=JAMAL, SUMAYAH
E4	1	AU=JAMAL, ZAHIRALI
E5	1	AU=JAMALA S
E6	1	AU=JAMALA S.
E7	1	AU=JAMALABAD
E8	4	AU=JAMALABAD VIKRAM R
E9	1	AU=JAMALABADI M H
E10	1	AU=JAMALABADI M.H.
E11	1	AU=JAMALABADI MH
E12	2	AU=JAMALADINI H

Enter P or PAGE for more
?s e5
>>>One or more prefixes are unsupported

```
>>>  or undefined in one [redacted] more files.
      S2        1  AU="JAM[redacted]A S"
?d s2
     Display 2/2/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

01211328   BIOSIS NO.: 000056021531
EVALUATION OF THE PROTEIN QUALITY OF 2 SELECTED VEGETABLE PROTEIN MIXTURES
 USING ALBINO RATS
AUTHOR: EASWARAN P P; GOPINATH S; *JAMALA S*; DEVADAS R P
JOURNAL: INDIAN J NUTR DIET 9 (6). 1972 (RECD 1973) 327-330. 1972
FULL JOURNAL NAME: Indian Journal of Nutrition and Dietetics
CODEN: IJNDA
RECORD TYPE: Citation
DESCRIPTORS: MAIZE BENGAL GRAM GROUNDNUT GREEN GRAM SKIM MILK
CONCEPT CODES:
  13224   Nutrition-Proteins, Peptides and Amino Acids (1972- )
  13518   Food Technology-Dairy Products
  13530   Food Technology-Evaluations of Physical and Chemical Properties
             (1970- )
  13534   Food Technology-Synthetic, Supplemental and Enrichment Foods
             (1970- )

                                        -more-
?s e6
>>>One or more prefixes are unsupported
>>>  or undefined in one or more files.
      S3        1  AU="JAMALA S."
?d s3
     Display 3/2/1     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2001 Elsevier Science B.V. All rts. reserv.

00475925     EMBASE No: 1976031464
 Nutritional evaluation of a maize based indigenous infant food,
'Kuzhandai Amudhu'
  Devadas R.P.; *Jamala S.*; Chandrasekhar U.; Murthy N.K.
  Sri Avinashilingam Home Sci. Coll. Women, Coimbatore  India
  INDIAN J.NUTR.DIET.  1974, 11/5 (257-263)
  CODEN: INDIA
  DOCUMENT TYPE: Journal
  LANGUAGE: ENGLISH
DRUG DESCRIPTORS:
*protein
MEDICAL DESCRIPTORS:
*growth; *infant; *infant feeding; *maize; *feeding behavior; *nutritional
status
methodology; prevention
CAS REGISTRY NO.: 67254-75-5 (protein)

                                        -more-
?s endothelin B receptor
      S4     3497  ENDOTHELIN B RECEPTOR
?s s4 and molecule?
            3497  S4
         1096369  MOLECULE?
      S5       74  S4 AND MOLECULE?
?s s5 and antisense
              74  S5
           94843  ANTISENSE
      S6        0  S5 AND ANTISENSE
?s s5 and antagonis?
              74  S5
         1167812  ANTAGONIS?
      S7       31  S5 AND ANTAGONIS?
?rd
```

>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
      S8   12 RD (unique items)
?t s8/5/all

8/5/1   (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

01503472   99188542
Downregulation of intercellular adhesion *molecule*-1 expression on human synovial fibroblasts by endothelin-1.
Iwabuchi H; Kasama Y; Hanaoka R; Miwa Y; Hatano Y; Kobayashi K; Mori Y; Negishi M; Ide H; Adachi M
First Department of Internal Medicine, Showa University School of Medicine, Tokyo, Japan.
J Rheumatol; 26(3):522-31 1999 ISSN 0315-162X Journal Code: JWX
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 199906
Subfile: L; M MEDL/99188542
OBJECTIVE: To study the effect of endothelin-1 (ET-1) on the expression of intercellular adhesion *molecule* -1 (ICAM-1) by synovial fibroblasts derived from individuals with rheumatoid arthritis (RA) or osteoarthritis (OA). METHODS: The expression of ICAM-1 protein and the abundance of ICAM-1 mRNA in synovial fibroblasts derived from individuals with RA or OA, or healthy controls, was assessed by flow cytometry and Northern blot analysis, respectively. mRNA expression of ET type A (ETA) and ET type B (ETB) receptors was assessed by reverse transcription polymerase chain reaction. RESULTS: Tumor necrosis factor-alpha (TNF-alpha) increased the expression of ICAM-1 by RA and OA fibroblasts. While ET-1 alone had no significant effect on ICAM-1 expression by either cell type, it inhibited the TNF-alpha induced increase in ICAM-1 expression, and this effect was more marked in RA fibroblasts. TNF-alpha also increased the amount of ICAM-1 mRNA in both cell types, and ET-1 inhibited this increase to a greater extent in RA fibroblasts than in OA fibroblasts. This inhibitory effect of ET-1 was reversed by addition of specific *antagonist* of ETA receptor. mRNA expression of ETA and ETB receptors was significantly greater in RA fibroblasts stimulated with TNF-alpha or even medium alone than in OA fibroblasts. CONCLUSION: These results suggest that ICAM-1 expression by fibroblasts is regulated not only by proinflammatory cytokines such as TNF-alpha and interleukin-1beta, but also by the vasoactive peptide ET-1, and that ET-1 may play an important role in inflammatory responses, especially in rheumatoid synovitis.
Tags: Female; Human; Male; Support, Non-U.S. Gov't
Major Descriptors: Endothelin-1--Pharmacology--PD; *Fibroblasts --Drug Effects--DE; *Intercellular Adhesion *Molecule*-1--Biosynthesis--BI; *Synovial Membrane--Drug Effects--DE
Minor Descriptors: Aged; Arthritis, Rheumatoid--Metabolism--ME; Cells, Cultured; Cycloheximide--Pharmacology--PD; Dactinomycin--Pharmacology--PD; Dose-Response Relationship, Drug; Down-Regulation (Physiology); DNA Primers --Chemistry--CH; Fibroblasts--Metabolism--ME; Flow Cytometry; Immunoenzyme Techniques; Intercellular Adhesion *Molecule*-1--Genetics--GE; Interleukin-1--Pharmacology--PD; Middle Age; Osteoarthritis--Metabolism--ME ; Receptors, Endothelin--Genetics--GE; Receptors, Endothelin--Metabolism --ME; Reverse Transcriptase Polymerase Chain Reaction; RNA, Messenger --Biosynthesis--BI; Synovial Membrane--Cytology--CY; Synovial Membrane --Metabolism--ME; Tumor Necrosis Factor--Pharmacology--PD
CAS Registry No.: 0 (endothelin A receptor); 0 (endothelin B receptor) ; 0 (DNA Primers); 0 (Endothelin-1); 0 (Interleukin-1); 0 (Receptors, Endothelin); 0 (RNA, Messenger); 0 (Tumor Necrosis Factor)

; 126547-89-5 (Intercellular Adhesion Molecule-1); 50-76-0 (Dactinomycin); 66-81-9 (Cycloheximide)

8/5/2 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit

01355165 97359926
Design of a potent combined pseudopeptide endothelin-A/endothelin-B receptor *antagonist* , Ac-DBhg16-Leu-Asp-Ile-[NMe]Ile-Trp21 (PD 156252): examination of its pharmacokinetic and spectral properties.
Cody WL; He JX; Reily MD; Haleen SJ; Walker DM; Reyner EL; Stewart BH; Doherty AM
Department of Chemistry, Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, Michigan 48105, USA. codyw@aa.wl.com
J Med Chem; 40(14):2228-40 1997 ISSN 0022-2623 Journal Code: J0F
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 199709
Subfile: L; M; X MEDL/97359926
The endothelins (ETs) are a family of bicyclic 21-amino acid peptides that are potent and prolonged vasoconstrictors. It has been shown that highly potent combined ETA/ETB receptor *antagonists* can be developed from the C-terminal hexapeptide of ET (His16-Leu17-Asp18-Ile19-Ile20-Trp21), such as Ac-(D)Dip16-Leu-Asp-Ile-Ile-Trp21 (PD 142893) and Ac-DBhg16-Leu-Asp-Ile-Ile-Trp21 (PD 145065). However, these compounds are relatively unstable to enzymatic proteolysis as determined in an in vitro rat intestinal perfusate assay. This instability is thought to be due to carboxypeptidase activity. In fact, incubation of PD 145065 with carboxypeptidase inhibitors greatly increased its half-life in rat intestinal perfusate. By performing a reduced amide bond and N-methyl amino acid scan, it was discovered that N-methylation of Ile-20 resulted in a compound (Ac-DBhg16-Leu-Asp-Ile-[NMe]Ile-Trp21, PD 156252) that retained full receptor affinity at both endothelin receptor subtypes along with enhanced proteolytic stability and cellular permeability. Interestingly, N-methylation of this bond allows the cis configuration to be readily accessible which greatly alters the preferred structure of the entire *molecule* and may be responsible for the observed enhanced metabolic stability.
Tags: Animal; Human; In Vitro
Major Descriptors: Muscle, Smooth, Vascular--Physiology--PH; *Oligopeptides--Chemical Synthesis--CS; *Receptors, Endothelin--*Antagonists* and Inhibitors--AI
Minor Descriptors: Amino Acid Sequence; Drug Design; Endothelin-1--Chemistry--CH; Femoral Artery; Kinetics; Molecular Sequence Data; Muscle Contraction--Drug Effects--DE; Muscle, Smooth, Vascular--Drug Effects--DE; Nuclear Magnetic Resonance; Oligopeptides--Chemistry--CH; Oligopeptides--Pharmacology--PD; Oligopeptides--Pharmacokinetics--PK; Protein Conformation; Pulmonary Artery; Rabbits; Rats; Renal Circulation--Drug Effects--DE; Structure-Activity Relationship; Tumor Cells, Cultured
CAS Registry No.: 0 (endothelin A receptor); 0 (endothelin B receptor); 0 (Endothelin-1); 0 (Oligopeptides); 0 (PD 156252); 0 (Receptors, Endothelin); 143037-36-9 (PD 142893)

8/5/3 (Item 3 from file: 159)
DIALOG(R)File 159:Cancerlit

01241446 96205044
Distinct stages of melanocyte differentiation revealed by anlaysis of nonuniform pigmentation patterns.
Yoshida H; Kunisada T; Kusakabe M; Nishikawa S; Nishikawa SI
Department of Molecular Genetics, Faculty of Medicine, Kyoto University, Japan.
Development; 122(4):1207-14 1996 ISSN 0950-1991 Journal Code: ECW

Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 199607
Subfile: L; M MEDL/96205044

The injection of an *antagonistic* anti-murine c-kit monoclonal antibody ACK2 during mouse embryonic development produced three distinctive pigmentation patterns on the coat of the offspring. Pattern 1 consisted of pigmentation in craniofacial and caudal regions and was induced by an ACK2 injection between 9.5 and 11.5 days post coitum (dpc). In pattern 2, the entire coat was unpigmented and was induced by the injection at around 13.0 dpc. Pattern 3 consisted of pigmented patches spreading ventrolaterally from the dorsoanterior trunk regions towards the anterior and posterior directions and it was induced by ACK2 administered at 14.5-15.0 dpc. We investigated the embryological basis of these nonuniform pigmentation patterns to elucidate the process of melanoblast differentiation between lineage commitment and colonization into developing hair follicles. The results showed the following. (1) Melanocyte differentiation at the embryonic stage from 10.5 to 12.5 dpc progresses in a spatially nonuniform fashion, being faster in the craniofacial and caudal regions than in the trunk; pattern 1 reflects this. (2) Melanoblasts are activated to proliferate synchronously upon entering into the epidermis; pattern 2 correlates with this process. (3) c-kit functions as a survival signal for proliferating melanoblasts in the epidermis. (4) The melanoblasts that enter developing hair follicles can survive without a c-kit signal; pattern 3 essentially represents the hair follicles colonized by these cells. Analysis of the melanoblast distribution of ls/ls embryos that bear a loss-of-function mutation in the endothelin 3 gene suggested that endothelin 3 is required for early melanoblast differentiation before entering into the epidermis, whereas proliferation in the epidermis takes place without this *molecule*. Based on these data, we propose 4 distinct steps of embryonic melanocyte differentiation: (1) migration in the dermis, which requires both c-kit and endothelin 3; (2) a state before epidermal entry that is resistant to anti-c-kit mAb; (3) cell proliferation after entering the epidermal layer, which requires c-kit and endothelin receptor B but not endothelin 3 and (4) integration into developing hair follicles, which renders melanoblasts resistant to anti-c-kit mAb. Thus, melanoblast differentiation proceeds by alternately repeating c-kit -dependent and c-kit-independent stages and c-kit functions as a survival factor for the proliferating melanoblasts.

Tags: Animal; Female; Support, Non-U.S. Gov't

Major Descriptors: *Hair Follicle--Embryology--EM; *Melanocytes--Cytology --CY; *Proto-Oncogene Protein c-kit--Analysis--AN; *Skin Pigmentation

Minor Descriptors: Antibodies, Monoclonal--Administration and Dosage--AD; Cell Differentiation; Cell Division; Cell Movement; Endothelins--Physiology --PH; Epidermis--Chemistry--CH; Epidermis--Embryology--EM; Fetal Development; Hair Follicle--Cytology--CY; Isomerases--Analysis--AN; Mice; Mice, Inbred Strains; Mice, Mutant Strains; Pregnancy; Receptors, Endothelin--Physiology--PH

CAS Registry No.: 0 (endothelin B receptor); 0 (Antibodies, Monoclonal); 0 (Endothelins); 0 (Receptors, Endothelin)

Enzyme No.: EC 2.7.11.- (Proto-Oncogene Protein c-kit); EC 5. (Isomerases); EC 5.3.2.- (dopachrome oxidoreductase)

8/5/4 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

07739795 EMBASE No: 1999222862

Endothelin-1 enhances neutrophil adhesion to human coronary artery endothelial cells: Role of ET(A) receptors and platelet-activating factor

Zouki C.; Baron C.; Fournier A.; Filep J.G.
J.G. Filep, Maisonneuve-Rosemont Hospital, Department of Medicine, University of Montreal, Montreal, Que. H1T 2M4 Canada
AUTHOR EMAIL: filepj@ere.umontreal.ca

British Journal of Pharmacology (BR. J. PHARMACOL.) (United Kingdom)
1999, 127/4 (969-979)

CODEN: BJPCB ISSN: 0[redacted]-1188
DOCUMENT TYPE: Journal[redacted]rticle
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 52

1. The potent coronary vasoconstrictor, endothelin-1 (ET-1) may also regulate neutrophil traffic into tissues. The aim of the present study was to characterize the endothelin receptors responsible and to investigate the underlying mechanisms. 2. ET-1 (1 nM-1 muM) markedly enhanced attachment of human neutrophils to lipopolysaccharide-, and to a lesser extent, to ET-1-activated human coronary artery endothelial cells (HCAEC). This can partially be blocked by monoclonal antibodies against E-selectin, L-selectin or CD18, whereas combination of the three antibodies inhibited adhesion by ~83%. Increases in neutrophil adhesion evoked by ET-1 were also blocked by the platelet-activating factor (PAF) *antagonists*, BN 52021 (50 muM) and WEB 2086 (10 muM). 3. ET-1 downregulated the expression of L-selectin and upregulated expression of CD11b/CD18 and CD45 on the neutrophil surface and induced gelatinase release with EC$D5inf 0 values of ~2 nM. These actions of ET-1 were almost completely prevented by the ET(A) receptor *antagonist* FR 139317 (1 muM) and the ET(A)/ET(B) receptor *antagonist* bosentan (10 muM), whereas the ET(B) receptor *antagonist* BQ 788 (1 muM) had no effect. ET-1 slightly increased the expression of E-selectin and ICAM-1 on HCAEC, that was prevented by BQ 788, but not by FR 139317. 4. Receptor binding studies indicated the presence of ET(B) receptors (K(D): 40 pM) on phosphoramidon-treated HCAEC and the predominant expression of ET(A) receptors (K(D): 38 pM) on neutrophils. 5. These results indicate that promotion by ET-1 of neutrophil adhesion to HCAEC is predominantly mediated through activation of ET(A) receptors on neutrophils and subsequent generation of PAF.

BRAND NAME/MANUFACTURER NAME: fr 139317/Fujisawa/Japan; bq 788/Calbiochem Novabiochem/United States; bn 52021/Beaufour/France; web 2086/Boehringer Ingelheim/Germany
MANUFACTURER NAMES: Hoffmann La Roche/Switzerland; Fujisawa/Japan; Calbiochem Novabiochem/United States; Beaufour/France; Boehringer Ingelheim /Germany
DRUG DESCRIPTORS:
*endothelin 1--pharmacology--pd
vasoconstrictor agent--pharmacology--pd; monoclonal antibody; ginkgolide b --pharmacology--pd; apafant--pharmacology--pd; l selectin--endogenous compound--ec; cd11b antigen--endogenous compound--ec; cd18 antigen --endogenous compound--ec; cd45 antigen--endogenous compound--ec; gelatinase--endogenous compound--ec; 2 [[2 [[2 [[(hexahydro 1h azepin 1 yl)carbonyl]amino] 4 methylpentanoyl]amino] 3 (1 methyl 1h indol 3 yl)propionyl]amino] 3 (2 pyridyl)propionic acid--pharmacology--pd; bosentan --pharmacology--pd; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine--pharmacology--pd; endothelial leukocyte adhesion *molecule* 1--endogenous compound--ec; intercellular adhesion *molecule* 1--endogenous compound--ec; *endothelin b receptor*--endogenous compound--ec; endothelin a receptor--endogenous compound--ec
MEDICAL DESCRIPTORS:
neutrophil; leukocyte adherence; endothelium cell; human; human cell; article; priority journal
CAS REGISTRY NO.: 99796-69-7 (ginkgolide b); 105219-56-5 (apafant); 126880-86-2 (l selectin); 9040-48-6 (gelatinase); 142375-60-8 (2 [[2 [[2 [[(hexahydro 1h azepin 1 yl)carbonyl]amino] 4 methylpentanoyl]amino] 3 (1 methyl 1h indol 3 yl)propionyl]amino] 3 (2 pyridyl)propionic acid); 156161-89-6 (n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine); 128875-25-2 (endothelial leukocyte adhesion *molecule* 1); 126547-89-5 (intercellular adhesion *molecule* 1)
SECTION HEADINGS:
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

07601250 EMBASE No: 1999099411

Endothelin-1 enhances vascular cell adhesion *molecule*-1 expression in tumor necrosis factor alpha-stimulated vascular endothelial cells

Ishizuka T.; Takamizawa-Matsumoto M.; Suzuki K.; Kurita A.
T. Ishizuka, Division of Biomedical Engineering, National Defense Medical College, Research Institute, 3-2 Namiki, Tokorozawa, Saitama Japan

European Journal of Pharmacology (EUR. J. PHARMACOL.) (Netherlands) 1999, 369/2 (237-245)
CODEN: EJPHA ISSN: 0014-2999
PUBLISHER ITEM IDENTIFIER: S0014299999000424
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 37

Vascular cell adhesion *molecule*-1 (VCAM-1) is a mononuclear leukocyte-selective adhesion *molecule* that is expressed in human vascular endothelial cells at sites of local inflammation. It participates in local endothelial-monocyte interactions during the initiation of atherosclerosis. In the present study, endothelin alone did not induce the surface expression and mRNA accumulation of VCAM-1 in human vascular endothelial cells, but inhibition of endogenous nitric oxide (NO) by N(G)-monomethyl-l-arginine enhanced the surface expression and mRNA accumulation of VCAM-1 stimulated by endothelin-1. It is conceivable that in human vascular endothelial cells, stimulation of an endothelin receptor results in the production of nitric oxide (NO), suppressing the expression of VCAM-1. Endothelin-1 enhanced the surface expression and mRNA accumulation of VCAM-1 in cells treated with tumor necrosis factor alpha (TNF-alpha). The enhancement by endothelin-1 may be explained by the inhibitory effect of TNF-alpha on endothelin-induced NO production. Pretreatment with BQ788 (an endothelin ET(B) receptor *antagonist*) or inhibitors of nuclear factor kappa B (NF-kappaB) activation completely diminished the synergistic enhancement of VCAM-1 expression by endothelin-1 in TNF-alpha-stimulated vascular endothelial cells, both at the protein and mRNA levels. These findings suggest that the synergistic enhancement of VCAM-1 expression by TNF-alpha and endothelin ET(B) receptor stimulation may be augmented by the induction of NF-kappaB binding activity in human vascular endothelial cells. Copyright (C) 1999 Elsevier Science B.V.

BRAND NAME/MANUFACTURER NAME: bq 3020/Banyu/Japan; bq 610; bq 788
MANUFACTURER NAMES: Banyu/Japan; Genzyme/United States; Sigma/United States
DRUG DESCRIPTORS:
*endothelin 1--pharmacology--pd; *endothelin 1--drug comparison--cm; *endothelin 1--drug combination--cb; *vascular cell adhesion *molecule* 1 --endogenous compound--ec; *tumor necrosis factor alpha--pharmacology--pd; *tumor necrosis factor alpha--drug comparison--cm; *tumor necrosis factor alpha--drug combination--cb; **endothelin b receptor*--endogenous compound --ec
messenger RNA--endogenous compound--ec; nitric oxide--endogenous compound --ec; n(g) methylarginine; n acetylendothelin 1 [6-21][11,15 alanine] --pharmacology--pd; n acetylendothelin 1 [6-21][11,15 alanine]--drug comparison--cm; endothelin 2--pharmacology--pd; endothelin 2--drug comparison--cm; endothelin 3--pharmacology--pd; endothelin 3--drug comparison--cm; bq 610--pharmacology--pd; bq 610--drug interaction--it; bq 610--drug dose--do; bq 610--drug comparison--cm; bq 610--drug combination --cb; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine--pharmacology--pd; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine--drug interaction--it; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine--drug dose--do; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine--drug comparison--cm; n (2,6

dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine--drug combination--cb; 3 aminobenzamide--pharmacology--pd; 3 aminobenzamide--drug comparison--cm; 3 aminobenzamide--drug combination--cb; acetylcysteine--pharmacology--pd; acetylcysteine--drug interaction--it; acetylcysteine--drug comparison--cm; acetylcysteine--drug combination--cb; pyrrolidine dithiocarbamate --pharmacology--pd; pyrrolidine dithiocarbamate--drug comparison--cm; pyrrolidine dithiocarbamate--drug combination--cb
MEDICAL DESCRIPTORS:
*vascular endothelium
endothelium cell; in vitro study; protein expression; reverse transcription polymerase chain reaction; immunofluorescence; human; female; normal human; controlled study; human cell; article; priority journal
CAS REGISTRY NO.: 10102-43-9 (nitric oxide); 156706-47-7, 17035-90-4 (n(g) methylarginine); 143113-45-5 (n acetylendothelin 1 [6-21][11,15 alanine]); 141595-53-1 (bq 610); 156161-89-6 (n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine); 3544-24-9 (3 aminobenzamide); 616-91-1 (acetylcysteine)
SECTION HEADINGS:
018 Cardiovascular Diseases and Cardiovascular Surgery
002 Physiology
037 Drug Literature Index
008 Neurology and Neurosurgery

8/5/6 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE

07382442 EMBASE No: 1998294613
Investigations of structural requirements for endothelin *antagonism*
Van der Walle C.F.; Barlow D.J.
D.J. Barlow, Pharmacy Department, King's College, London SW3 6LX United Kingdom
Current Medicinal Chemistry (CURR. MED. CHEM.) (Netherlands) 1998, 5/4 (321-335)
CODEN: CMCHE ISSN: 0929-8673
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 78

Following the isolation of the vasoactive peptide, endothelin (ET), considerable effort has been expended in the development of ET *antagonists*, some of which have recently been proved to be promising therapeutic agents. Their clinical potential, however, is often limited because of a peptidic nature or a non-selective ET(A)/ET(B) receptor *antagonism*. While many non-peptide ET *antagonists* are optimised ad hoc from a lead compound found during a compound screening program, directing the development of a *molecule* towards a selectivity for the ETA or ETB receptor rests upon the elucidation of the respective receptor-binding conformation of ET-1 and ET-3, or a template structure derived from a peptide *antagonist* whose structure/activity relationship is well characterised. This review focuses on peptide ET *antagonists* whose structure/activity relationships are well characterised and so provides some insight to the conformational criteria required of putative ET(A) or ET(B) receptor selective *antagonists*. Although the conformation of ET has been previously reported in depth on many occasions a brief summary is provided here in order to relate the structure/activity relationships of the ET *antagonists* to the structure of ET. The list of ET *antagonists* discussed here is not comprehensive, since the emphasis for the review has been to focus on studies where structural data were obtained which shed light on the receptor binding conformation(s) of endothelin.

BRAND NAME/MANUFACTURER NAME: bq 123; bq 153; ipi 725; be 18257b; be 18257a
DRUG DESCRIPTORS:
*endothelin--endogenous compound--ec; *endothelin a receptor--endogenous

compound--ec; *receptor subtype--endogenous compound--ec; *endothelin b receptor*--endogenous compound--ec; *endothelin receptor *antagonist*--drug analysis--an; *endothelin receptor *antagonist*--drug comparison--cm; *endothelin receptor *antagonist*--drug development--dv; *endothelin receptor *antagonist*--pharmacology--pd
cyclopeptide--drug analysis--an; cyclopeptide--drug comparison--cm; cyclopeptide--drug development--dv; cyclopeptide--pharmacology--pd; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug comparison--cm; cyclo(dextro tryptophyl dextro cysteic acid prolyl dextro valylleucyl)--drug comparison--cm; cyclo(dextro glutamylalanyl dextro allo isoleucylleucyl dextro tryptophyl)--drug analysis--an; cyclo(dextro glutamylalanyl dextro allo isoleucylleucyl dextro tryptophyl)--drug comparison--cm; cyclo(dextro glutamylalanyl dextro allo isoleucylleucyl dextro tryptophyl)--drug development--dv; cyclo(dextro glutamylalanyl dextro allo isoleucylleucyl dextro tryptophyl)--pharmacology--pd; pentapeptide--drug analysis--an; pentapeptide--drug comparison--cm; pentapeptide--drug development--dv; pentapeptide--pharmacology--pd; tripeptide--drug analysis--an; tripeptide--drug comparison--cm; tripeptide--drug development--dv; tripeptide--pharmacology--pd; unclassified drug
MEDICAL DESCRIPTORS:
*drug receptor binding
binding affinity; circular dichroism; molecular model; drug synthesis; in vitro study; reaction analysis; drug design; nuclear magnetic resonance spectroscopy; amino acid sequence; human; nonhuman; review
DRUG TERMS (UNCONTROLLED): ipi 725--drug analysis--an; ipi 725--drug comparison--cm; ipi 725--drug development--dv; ipi 725--pharmacology--pd; cyclo(dextro glutamylalanyl dextro valylleucyl dextro tryptophyl)--drug analysis--an; cyclo(dextro glutamylalanyl dextro valylleucyl dextro tryptophyl)--drug comparison--cm; cyclo(dextro glutamylalanyl dextro valylleucyl dextro tryptophyl)--drug development--dv; cyclo(dextro glutamylalanyl dextro valylleucyl dextro tryptophyl)--pharmacology--pd
CAS REGISTRY NO.: 136553-81-6 (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)); 139346-17-1 (cyclo(dextro tryptophyl dextro cysteic acid prolyl dextro valylleucyl)); 136553-74-7 (cyclo(dextro glutamylalanyl dextro allo isoleucylleucyl dextro tryptophyl))
SECTION HEADINGS:
002 Physiology
008 Neurology and Nerosurgery
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

8/5/7 (Item 4 from file: 72)
DIALOG(R)File 72:EMBASE

06926895 EMBASE No: 1997211374
Endothelin: From *molecule* to man
Webb D.J.
D.J. Webb, Clinical Pharmacology Unit, Res.Unit, University of Edinburgh, Western General Hospital, Edinburgh EH4 2XU United Kingdom
British Journal of Clinical Pharmacology (BR. J. CLIN. PHARMACOL.) (United Kingdom) 1997, 44/1 (9-20)
CODEN: BCPHB ISSN: 0306-5251
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 84

Endothelin-1 is an endothelium-derived vasoconstrictor and co-mitogenic agent which acts as a local paracrine and autocrine mediator; and is the most potent and sustained vasoconstrictor and presser substance yet identified. On the basis of studies in healthy man, endothelin-1 is now known to play an important physiological role in maintaining peripheral vascular tone and blood pressure. Endothelin-1 also has actions which might influence the function of the heart, kidney and nervous system. However,

their physiological importance remains to be determined. Abnormalities of the endothelin system are now recognised to occur in a range of diseases associated with vasoconstriction, vasospasm and vascular hypertrophy and it appears that endothelin-1 may be causal, or at least contributory, in some of these pathophysiological processes. The use of endothelin receptor *antagonists* in experimental models of cardiovascular disease and in human clinical pharmacology studies has indicated a number of conditions - including hypertension, heart failure, acute renal failure, subarachnoid haemorrhage, and pulmonary hypertension - in which further clinical studies would be worthwhile. A number of peptide and orally-active non-peptide endothelin receptor *antagonists* are now under clinical investigation and further studies are now required in specific diseases to determine whether selective ET(A) or combined ET(A/B) receptor *antagonists* would be more effective. The discovery of endothelin-1, and the design of endothelin *antagonists*, has been among the most promising developments in cardiovascular medicine since the launch of ACE inhibitors 15 years ago. Major clinical trials are now needed to confirm the predicted benefits for endothelin *antagonists* in patients with cardiovascular disease.

BRAND NAME/MANUFACTURER NAME: bq 123; bq 788; tak 044
DRUG DESCRIPTORS:
*endothelin--endogenous compound--ec; *endothelin--pharmacology--pd; * endothelin receptor--endogenous compound--ec; *endothelin receptor *antagonist*--pharmacology--pd; *endothelin receptor *antagonist*--drug therapy--dt; *endothelin receptor *antagonist*--drug development--dv cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl) --pharmacology--pd; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug therapy--dt; dipeptidyl carboxypeptidase inhibitor --pharmacology--pd; dipeptidyl carboxypeptidase inhibitor--drug therapy--dt ; endothelin 1--endogenous compound--ec; endothelin 1--pharmacology--pd; endothelin 2--endogenous compound--ec; endothelin 2--pharmacology--pd; endothelin 3--pharmacology--pd; endothelin 3--endogenous compound--ec; endothelin a receptor--endogenous compound--ec; *endothelin b receptor* --endogenous compound--ec; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine --pharmacology--pd; phosphoramidon--pharmacology--pd; sarafotoxin s6c --pharmacology--pd; tak 044--pharmacology--pd; thiorphan--pharmacology--pd
MEDICAL DESCRIPTORS:
*cardiovascular disease--drug therapy--dt; *cardiovascular disease --etiology--et; *cardiovascular system
acute kidney failure--etiology--et; article; blood pressure regulation; blood vessel tone; cardiovascular function; clinical pharmacology; congestive heart failure--etiology--et; congestive heart failure--drug therapy--dt; gene expression; human; hypertension--etiology--et; nonhuman; pathophysiology; physiology; pressor response; priority journal; pulmonary hypertension--etiology--et; subarachnoid hemorrhage--etiology--et; vasoconstriction
CAS REGISTRY NO.: 136553-81-6 (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)); 156161-89-6 (n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine); 36357-77-4 (phosphoramidon); 116495-45-5 (sarafotoxin s6c); 157380-72-8 (tak 044); 76721-89-6 (thiorphan)
SECTION HEADINGS:
002 Physiology
005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

8/5/8 (Item 5 from file: 72)
DIALOG(R)File 72:EMBASE

06743991 EMBASE No: 1997025467
ICAM-1 expression on cardiac myocytes and aortic endothelial cells via

their specific endothelin receptor subtype

Hayasaki Y.; Nakajima M.; Kitano Y.; Iwasaki T.; Shimamura T.; Iwaki K.
M. Nakajima, Discovery Research Laboratories II, Shionogi and Co Ltd, 3-1-1 Futaba-cho, Toyonaka, Osaka 561 Japan

Biochemical and Biophysical Research Communications (BIOCHEM. BIOPHYS. RES. COMMUN.) (United States) 1996, 229/3 (817-824)
CODEN: BBRCA ISSN: 0006-291X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 29

Endothelin-1 (ET-1) and Endothelin-3 (ET-3) increased the expression of intercellular adhesion *molecule*-1 (ICAM-1) on rat neonatal cultured cardiac myocytes and rat aortic endothelial cells. ET-1-induced ICAM-1 expression on cardiac myocytes was inhibited by a selective ET(B) receptor *antagonist*, S-0139, but not by a selective ET(B) receptor *antagonist*, BQ788. ET-3-induced ICAM-1 expression on endothelial cells was inhibited by BQ788 but not by S-0139. Protein kinase C (PKC) inhibitor staurosporine inhibited ETs-induced ICAM-1 expression on both cell types. Treatment of the cells with ETs increased neutrophil adhesion, which was inhibited by S-0139 and staurosporine on cardiac myocytes and by BQ788 and staurosporine on endothelial cells. These results suggest that ETs induce neutrophil adhesion to cardiac myocytes and aortic endothelial cells by increasing ICAM-1 expression, which mediate via ET(A) receptor on cardiac myocytes and via ET(B) receptor on aortic endothelial cells. ICAM-1 expression induced by activation of ET(A) and ET(B) receptors appears to be mediated through die PKC pathway.

DRUG DESCRIPTORS:
*endothelin a receptor--endogenous compound--ec; **endothelin b receptor* --endogenous compound--ec; *endothelin receptor--endogenous compound--ec; * intercellular adhesion *molecule* 1--endogenous compound--ec
endothelin 1; endothelin 3; endothelin a receptor *antagonist*; endothelin b receptor *antagonist*; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine; protein kinase c inhibitor; receptor subtype--endogenous compound--ec; staurosporine
MEDICAL DESCRIPTORS:
*antigen expression; *heart muscle cell; *vascular endothelium
animal cell; aorta; article; controlled study; leukocyte adherence; neutrophil; newborn; nonhuman; priority journal; rat
CAS REGISTRY NO.: 126547-89-5 (intercellular adhesion *molecule* 1); 156161-89-6 (n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine); 62996-74-1 (staurosporine)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

8/5/9 (Item 6 from file: 72)

06687514 EMBASE No: 1996352435

Endothelin receptors and atherosclerosis: A potential target for therapeutic intervention

Kowala M.C.
Department of Biochemistry, Bristol-Myers Squibb, Pharmaceutical Research Institute, PO Box 4000,Princeton, NJ 08543-4000 United States

Expert Opinion on Investigational Drugs (EXPERT OPIN. INVEST. DRUGS) (United Kingdom) 1996, 5/11 (1495-1508)
CODEN: EOIDE ISSN: 1354-3784
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Endothelin (ET) is a powerful vasoconstrictor that affects vascular tone and blood pressure; however, recent evidence suggests that ET acts as an autocrine or paracrine factor and plays a role in the pathogenesis of

atherosclerosis. In human and in animal models, elevated plasma ET concentrations are associated with hypercholesterolaemia and atherosclerosis. ET and its receptors are located in endothelial cells, macrophages and smooth muscle cells of atherosclerotic and arteriosclerotic lesions. In vitro, endothelial cells, macrophages and smooth muscle cells synthesise ET and express ET receptors. Oxidised low density lipoprotein (LDL), growth factors, vasoactive peptides, and cytokines induce ET gene expression and protein synthesis. Conversely ET stimulates the synthesis of growth factors, inflammatory mediators, chemokines and adhesion *molecules* . In animal models, ET receptor *antagonists* decrease fatty streak progression during hypercholesterolaemia, and inhibit the formation of a fibrous neointima following arterial balloon catheter injury. It appears likely that ET indirectly promotes several phases of atherogenesis such as monocyte diapedesis into the artery wall, and the migration and proliferation of vascular smooth muscle cells. In summary, ET appears to be intricately involved in the elaboration of paracrine and autocrine factors mediating inflammation and wound healing. Pharmacological blockade of ET receptors inhibits the development of vascular lesions as a result of either hypercholesterolaemia or physical injury. Thus, it is possible that ET receptor *antagonists* could be used therapeutically to treat human vascular diseases such as atherosclerosis.

BRAND NAME/MANUFACTURER NAME: bq 123; bms 182874; sb 209670; fr 139317
DRUG DESCRIPTORS:
*endothelin--endogenous compound--ec; *endothelin--pharmacology--pd; * endothelin receptor--endogenous compound--ec; *endothelin receptor *antagonist*--pharmacology--pd
2 ((2 ((2 (((hexahydro 1h azepin 1 yl)carbonyl)amino) 4 methylpentanoyl)amino) 3 (1 methyl 1h indol 3 yl)propionyl)amino) 3 (2 pyridyl)propionic acid--pharmacology--pd; 3 (2 carboxymethoxy 4 methoxyphenyl) 1 (3,4 methylenedioxyphenyl) 5 propoxy 2 indancarboxylic acid--pharmacology--pd; 5 dimethylamino n (3,4 dimethyl 5 isoxazolyl) 1 naphthalenesulfonamide--pharmacology--pd; cell adhesion *molecule* --endogenous compound--ec; chemokine--endogenous compound--ec; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--pharmacology--pd; cytokine--endogenous compound--ec; endothelin 1--pharmacology--pd; endothelin 1--endogenous compound--ec; endothelin a receptor--endogenous compound--ec; endothelin a receptor *antagonist*--pharmacology--pd; *endothelin b receptor*--endogenous compound--ec; growth factor--endogenous compound--ec; low density lipoprotein--endogenous compound--ec; noradrenalin--pharmacology--pd; serotonin--pharmacology--pd; vasoactive intestinal polypeptide--endogenous compound--ec
MEDICAL DESCRIPTORS:
*atherogenesis--etiology--et; *atherosclerosis--etiology--et
animal model; artery intima proliferation; endothelium cell; gene expression; human; hypercholesterolemia--etiology--et; inflammation; macrophage; mediator; nonhuman; protein synthesis; review; smooth muscle fiber; wound healing
CAS REGISTRY NO.: 142375-60-8 (2 ((2 ((2 (((hexahydro 1h azepin 1 yl)carbonyl)amino) 4 methylpentanoyl)amino) 3 (1 methyl 1h indol 3 yl)propionyl)amino) 3 (2 pyridyl)propionic acid); 150355-66-1, 157659-79-5 (3 (2 carboxymethoxy 4 methoxyphenyl) 1 (3,4 methylenedioxyphenyl) 5 propoxy 2 indancarboxylic acid); 153042-42-3 (5 dimethylamino n (3,4 dimethyl 5 isoxazolyl) 1 naphthalenesulfonamide); 136553-81-6 (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)); 1407-84-7, 51-41-2 (noradrenalin); 50-67-9 (serotonin); 37221-79-7 (vasoactive intestinal polypeptide)
SECTION HEADINGS:
005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
022 Human Genetics
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

8/5/10 (Item 7 from file: 72)

06119173 EMBASE No: 1995149909

Role of positions 9 and 10 in the endothelin *molecule* for biological activity and discrimination of receptor subtypes

Miasiro N.; De Castiglione R.; Paiva A.C.M.
Departamento de Biofisica, Escola Paulista de Medicina, Rua Botucatu 862,04023-062 Sao Paulo, SP Brazil

European Journal of Pharmacology (EUR. J. PHARMACOL.) (Netherlands) 1995, 278/2 (103-109)
CODEN: EJPHA ISSN: 0014-2999
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The importance of residues 9 and 10 in endothelin-1 was assessed by studying the responses of the guinea-pig ileum to (Alasup 9)endothelin-1 and (Alasup 1sup 0)endothelin-1. Both analogues induced relaxation followed by contraction. (Alasup 9)Endothelin-1 showed similar ED$D5inf 0 values and maximum response to those of endothelin-1, whereas (Alasup 1sup 0)endothelin-1 showed a larger ED$D5inf 0 value and was a partial agonist. Endothelin-1 and (Alasup 1sup 0)endothelin-1 induced similar degrees of tachyphylaxis, whereas (Alasup 9)endothelin-1 induced very little tachyphylaxis, indicating that Lyssup 9 is important for inducing tachyphylaxis. Apamin inhibited the relaxation induced by endothelin-1 and (Alasup 9)endothelin-1 but not that induced by (Alasup 1sup 0)endothelin-1. BQ-123 (cyclo(D-Trp-D-Asp-Pro-D-Val-Leu), a specific endothelin ET(A) receptor *antagonist*, inhibited (Alasup 9)endothelin-1-, but not (Alasup 1sup 0)endothelin-1-induced contraction. Cross-tachyphylaxis and additivity studies indicated that (Alasup 9)endothelin-1, like endothelin-1, acts at the endothelin ET(A) receptor, whereas (Alasup 1sup 0)endothelin-1 behaved as an endotheIin ET(B) receptor agonist, like sarafotoxin S6c. Thus, the residue at position 10 plays a significant role in receptor activation and is a candidate for further exploration of receptor *antagonism*.

BRAND NAME/MANUFACTURER NAME: bq 123/banyu
MANUFACTURER NAMES: peptide institute/Japan; peninsula/United States; banyu ; sigma/United States
DRUG DESCRIPTORS:
*endothelin a receptor; **endothelin b receptor*; *receptor subtype; * endothelin 1--drug interaction--it; *endothelin 1--drug comparison--cm; * endothelin 1--pharmacology--pd; *endothelin derivative--drug comparison--cm ; *endothelin derivative--pharmacology--pd
partial agonist; angiotensin--pharmacology--pd; apamin--pharmacology--pd; apamin--drug interaction--it; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--pharmacology--pd; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug interaction--it; endothelin a receptor agonist--drug comparison--cm; endothelin a receptor agonist --pharmacology--pd; endothelin a receptor *antagonist*--pharmacology--pd; endothelin a receptor *antagonist*--drug interaction--it; endothelin b receptor agonist--pharmacology--pd; endothelin b receptor agonist--drug comparison--cm; endothelin receptor agonist--pharmacology--pd; endothelin receptor agonist--drug comparison--cm; sarafotoxin s6c--drug comparison--cm ; sarafotoxin s6c--pharmacology--pd; unclassified drug
MEDICAL DESCRIPTORS:
*ileum
agonist; animal tissue; article; concentration response; controlled study; drug inhibition; female; guinea pig; male; nonhuman; priority journal; smooth muscle contraction; smooth muscle relaxation; tachyphylaxis
DRUG TERMS (UNCONTROLLED): endothelin 1 (10 alanine)--drug comparison--cm; endothelin 1 (10 alanine)--pharmacology--pd; endothelin 1 (9 alanine) --pharmacology--pd; endothelin 1 (9 alanine)--drug comparison--cm; endothelin 1 (9 alanine)--drug interaction--it
CAS REGISTRY NO.: 11128-99-7, 1407-47-2 (angiotensin); 24345-16-2 (apamin); 136553-81-6 (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)); 116495-45-5 (sarafotoxin s6c)
SECTION HEADINGS:

048 Gastroenterology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

8/5/11 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09973681 99312707
Synthesis and structure-activity relationship studies of new endothelin pseudopeptide analogues containing alkyl spacers.
Galoppini C; Giusti L; Macchia M; Hamdan M; Mazzoni MR; Calvani F; Rovero P
CNR-IMD, Laboratorio Sintesi Peptidica, Pisa, Italy.
Il Farmaco (ITALY) Apr 30 1999, 54 (4) p213-7, ISSN 0014-827X Journal Code: ACZ
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9910
Subfile: INDEX MEDICUS
We replaced the Asp18-Ile19 dipeptide of the C-terminal ET analogue Ph-Ph-CH2-O-N=CH-CO-Phe-Asp-Ile-Ile-Trp-OH by alkyl spacers of various lengths to investigate the role of the aminoacidic central portion of the *molecule* and to define the N-terminal and C-terminal pharmacophoric regions of this analogue. The side-chains of the central dipeptide have been shown to be irrelevant for the binding of the *molecule* to the receptor, but the distance between the two postulated sites of interaction of the ligand with the ETB receptor appears to be fundamental.
Tags: Animal; In Vitro; Male
Descriptors: Endothelins--Chemistry--CH; *Peptide Fragments --Chemical Synthesis--CS; *Receptors, Endothelin--*Antagonists* and Inhibitors--AI; Cerebellum--Drug Effects--DE; Cerebellum--Metabolism--ME; Ligands; Peptide Fragments--Chemistry--CH; Peptide Fragments--Metabolism--ME; Radioligand Assay; Rats; Rats, Sprague-Dawley; Structure-Activity Relationship
CAS Registry No.: 0 (endothelin B receptor); 0 (Endothelins); 0 (Ligands); 0 (Peptide Fragments); 0 (Receptors, Endothelin)

8/5/12 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09549418 98257814
Pharmacologic characterization of the novel, orally available endothelin-A--selective *antagonist* SB 247083.
Douglas SA; Nambi P; Gellai M; Luengo JI; Xiang JN; Brooks DP; Ruffolo RR Jr; Elliott JD; Ohlstein EH
Department of Cardiovascular, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406-0939, USA.
Journal of cardiovascular pharmacology (UNITED STATES) 1998, 31 Suppl 1 pS273-6, ISSN 0160-2446 Journal Code: K78
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9809
Subfile: INDEX MEDICUS
Competition radioligand binding with [125I]ET-1 at human cloned ETA and ETB receptors demonstrated ET-A selective affinity by SB 247083 (Ki 0.41 and 467 nM, respectively). Accordingly, similar competitive, functional ETA receptor *antagonism* was observed. In vitro, SB 247083 exhibited a Kb of 3.5 +/- 0.3 nM (ET-1--induced rat aortic contraction). SB 247083 was significantly less potent as a functional ETB *antagonist* (Kb 0.34 +/- 0.01 microM; S6c-induced rabbit pulmonary artery contraction). In contrast to ETB-selective and mixed ETA/B *antagonists*, and consistent with its ETA-selective profile, in vivo administration of SB 247083 was not associated with an elevation in plasma ET-1 levels. Pharmacodynamic and pharmacokinetic studies revealed that SB 247083 was effectively absorbed

from the gastrointestinal tract. A single bolus dose inhibited the hemodynamic actions of [illegible]-1 for up to 8 h, consistent with a *molecule* shown to be 46% bioavailable. Therefore, the present study demonstrates that SB 247083, a unique chemical entity, represents a potent class of nonpeptide, orally active ETA-selective *antagonists*.
Tags: Animal; Human
Descriptors: Benzofurans--Pharmacology--PD; *Propionic Acids --Pharmacology--PD; *Receptors, Endothelin--*Antagonists* and Inhibitors --AI; Aorta, Thoracic--Drug Effects--DE; Aorta, Thoracic--Metabolism--ME; Blood Pressure--Drug Effects--DE; CHO Cells; Endothelin-1--Metabolism--ME; Hamsters; Muscle Contraction--Drug Effects--DE; Muscle, Smooth, Vascular --Drug Effects--DE; Rabbits; Rats; Rats, Sprague-Dawley; Receptors, Endothelin--Metabolism--ME; Vasoconstrictor Agents--Pharmacology--PD; Viper Venoms--Pharmacology--PD
CAS Registry No.: 0 (endothelin A receptor); 0 (endothelin B receptor) ; 0 (sarafotoxins s6); 0 (Benzofurans); 0 (Endothelin-1); 0 (Propionic Acids); 0 (Receptors, Endothelin); 0 (SB 247083); 0 (Vasoconstrictor Agents); 0 (Viper Venoms)
?ds

Set	Items	Description
S1	1	AU="SCHNEIDER, R. J."
S2	1	AU="JAMALA S"
S3	1	AU="JAMALA S."
S4	3497	ENDOTHELIN B RECEPTOR
S5	74	S4 AND MOLECULE?
S6	0	S5 AND ANTISENSE
S7	31	S5 AND ANTAGONIS?
S8	12	RD (unique items)

```
?s s4 and cancer?
          3497  S4
       2718980  CANCER?
      S9    81  S4 AND CANCER?
?s s9 and treatment?
            81  S9
       5862395  TREATMENT?
     S10    15  S9 AND TREATMENT?
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S11     5  RD (unique items)
?t s11/5/all
```

11/5/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

10746253 BIOSIS NO.: 199799367398

Methylation of the 5' CpG island of the endothelin B receptor gene is common in human prostate *cancer*.

AUTHOR: Nelson Joel B(a); Lee Wen-Hsiang; Nguyen Son N; Jarrard David F; Brooks James D; Magnuson Scott R; Opgenorth Terry J; Nelson William G; Bova G Steven
AUTHOR ADDRESS: (a)James Buchanan Brady Urol. Inst., Dep. Urol., A344, Johns Hopkins Bayview Med. Cent., 4940 Easte**USA
JOURNAL: Cancer Research 57 (1):p35-37 1997
ISSN: 0008-5472
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Production of the potent vasoconstrictor endothelin-1 (ET-1) by

human prostate *cancer* cells accompanies prostate *cancer* progression in vivo. The predominant endothelin receptor expressed by normal prostate epithelium, ET-B, is not expressed by any of the established human prostate *cancer* cell lines, and ET-B binding is decreased on prostate *cancer* tissues. ET-B, which may mediate ET-1 clearance and may inhibit ET-1 secretion, is encoded by a gene that contains a 5' CpG island encompassing the transcriptional regulatory region. We examined this regulatory region of the ET-B, receptor gene (EDNRB) to determine whether hypermethylation of cytidine nucleotides accompanies decreased ET-B expression in human prostate *cancer*. We found somatic methylation of CpG island sequences in EDNRB in 5 of 5 human prostate *cancer* cell lines, 15 of 21 primary prostate *cancer* tissues, and 8 of 14 prostate *cancer* metastases (70% of samples overall). Normal tissues contained only unmethylated EDNRB. *Treatment* of human prostatic carcinoma cell line cultures with 5-azacytidine induced ET-B mRNA expression, suggesting that CpG island methylation changes might accompany the apparent transcriptional silencing of EDNRB in vivo.

DESCRIPTORS:
MAJOR CONCEPTS: Endocrine System (Chemical Coordination and Homeostasis); Genetics; Membranes (Cell Biology); Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics); Neurology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Reproductive System (Reproduction); Urology (Human Medicine, Medical Sciences)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
MISCELLANEOUS TERMS: Research Article; CPG ISLAND SEQUENCE METHYLATION; *ENDOTHELIN B RECEPTOR*; ENDOTHELIN B RECEPTOR GENE; EXPRESSION; NEOPLASTIC DISEASE; PROSTATE *CANCER*; REPRODUCTIVE SYSTEM DISEASE/MALE ; TRANSCRIPTIONAL ACTIVITY; TUMOR BIOLOGY; UROLOGIC DISEASE
CONCEPT CODES:
03508 Genetics and Cytogenetics-Human
10300 Replication, Transcription, Translation
10508 Biophysics-Membrane Phenomena
13012 Metabolism-Proteins, Peptides and Amino Acids
15506 Urinary System and External Secretions-Pathology
16506 Reproductive System-Pathology
17020 Endocrine System-Neuroendocrinology (1972-)
20506 Nervous System-Pathology
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
24006 Neoplasms and Neoplastic Agents-Biochemistry
BIOSYSTEMATIC CODES:
86215 Hominidae

11/5/2 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

06955089 EMBASE No: 1997239657
Cardiovascular and Renal. Eighth European meeting on hypertension
Danser A.H.J.
A.H.J. Danser, Erasmus University, Dr. Molewaterplein 50, 3015 GE Rotterdam Netherlands
Expert Opinion on Investigational Drugs (EXPERT OPIN. INVEST. DRUGS) (United Kingdom) 1997, 6/8 (1109-1112)
CODEN: EOIDE ISSN: 1354-3784
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 2

The Eighth European Meeting on Hypertension, held in Milan, Italy, was

attended by approximately 4000 people. The programme consisted of 120 presentations, 337 poster sessions, G invited lectures/debates (endothelin antagonists; cardiac renin-angiotensin system; *cancer* and hypertension; adducin; angiotensin converting enzyme (ACE) gene polymorphism; pulse pressure) and 2 plenary sessions on 'sleep apnea and hypertension' and '*treatment* of hypertension in the elderly'.

BRAND NAME/MANUFACTURER NAME: lu 135252; bq 123
DRUG DESCRIPTORS:
adducin--endogenous compound--ec; angiotensin--endogenous compound--ec; angiotensin--pharmacology--pd; angiotensin 1 receptor--endogenous compound --ec; angiotensin 2 receptor--endogenous compound--ec; angiotensin antagonist--pharmacology--pd; antihypertensive agent--pharmacology--pd; antihypertensive agent--drug therapy--dt; beta adrenergic receptor blocking agent--pharmacology--pd; bosentan--pharmacology--pd; calcium--drug therapy --dt; calcium--pharmacology--pd; calcium channel blocking agent --pharmacology--pd; candesartan--pharmacokinetics--pk; candesartan --pharmacology--pd; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--pharmacology--pd; dipeptidyl carboxypeptidase--endogenous compound--ec; enalapril--pharmacology--pd; endothelin--pharmacology--pd; endothelin--endogenous compound--ec; endothelin a receptor--endogenous compound--ec; endothelin a receptor antagonist--pharmacology--pd; *endothelin b receptor*--endogenous compound--ec; endothelin receptor antagonist--pharmacology--pd; furosemide--pharmacology--pd; icatibant --pharmacology--pd; losartan--pharmacology--pd; unclassified drug
MEDICAL DESCRIPTORS:
*hypertension--drug therapy--dt; *hypertension--etiology--et *cancer*; conference paper; genetic polymorphism; human; nonhuman; pulse pressure; renin angiotensin aldosterone system; sleep apnea syndrome; vascular endothelium
DRUG TERMS (UNCONTROLLED): lu 135252--pharmacology--pd
CAS REGISTRY NO.: 11128-99-7, 1407-47-2 (angiotensin); 7440-70-2 (calcium); 139481-59-7 (candesartan); 136553-81-6 (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)); 9015-82-1 (dipeptidyl carboxypeptidase); 75847-73-3 (enalapril); 54-31-9 (furosemide); 130308-48-4 (icatibant); 114798-26-4 (losartan)
SECTION HEADINGS:
003 Endocrinology
005 General Pathology and Pathological Anatomy
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

11/5/3 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

06555221 EMBASE No: 1996215888
Tumour blood flow modification by endothelin-related peptides in the rat HSN fibrosarcoma
Bell K.M.; Prise V.E.; Chaplin D.J.; Tozer G.M.
CRC Tumour Microcirculation Group, Gray Laboratory Cancer Res. Trust, Mount Vernon Hospital, PO Box 100,Northwood, Middlesex HA6 2JR United Kingdom
British Journal of Cancer (BR. J. CANCER) (United Kingdom) 1996, 74/SUPPL. XXVII (S161-S163)
CODEN: BJCAA ISSN: 0007-0920
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Modification of tissue blood flow and tissue vascular resistance was examined in the female CBH rat, bearing a HSN fibrosarcoma, following bolus intravenous administration of 1 nM kgsup -sup 1 endothelin-1 (ET-1) or 1 nM kgsup -sup 1 sarafotoxin S6c (SX6c), selective agonists for endothelin A (ETA) and B (ETB) receptors respectively. Blood flow was measured 15 min

after drug administration by the tissue uptake of sup 1sup sup 5I-labelled-iodoantipyrin ET-1 and SX6c produced increase in mean arterial blood pressure (MABP) of 52 mmHg and 42 mmHg respectively. Blood flow to the rumour was unaffected by ET-1 *treatment*, whereas blood flow to normal tissues was reduced, the exception being the heart and the brain in which flow was increased. In contrast, tumour blood flow following SX6c was significantly increased, whereas blood flow in normal tissues was either unaltered or reduced. Vascular resistance was increased in all tissues and the tumour by ET-1 demonstrating that the tumour vasculature was constricting via ETA receptor activation. SX6c however, did not modify tumour vascular resistance, whereas it increased vascular resistance in all normal tissues, suggesting that the tumour lacks a functional population of ETB receptors. This discrepancy may provide a means for selectively modifying tumour blood flow.

DRUG DESCRIPTORS:
*endothelin
endothelin a receptor--endogenous compound--ec; *endothelin b receptor*
--endogenous compound--ec; iodophenazone; sarafotoxin s6c
MEDICAL DESCRIPTORS:
*fibrosarcoma; *tumor blood flow
animal experiment; animal model; animal tissue; brain blood flow;
conference paper; controlled study; coronary artery blood flow; female;
mean arterial pressure; nonhuman; priority journal; rat; vascular
resistance; vasoconstriction
CAS REGISTRY NO.: 129-81-7 (iodophenazone); 116495-45-5 (sarafotoxin s6c)
SECTION HEADINGS:
  005 General Pathology and Pathological Anatomy
  016 *Cancer*

11/5/4 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE

05281256 EMBASE No: 1993049341
Endothelins - From receptors to medicine
Miller R.C.; Pelton J.T.; Huggins J.P.
Marion Merrell Dow Res. Institute, 16 Rue d'Ankara,67084 Strasbourg France
Trends in Pharmacological Sciences (TRENDS PHARMACOL. SCI.) (United Kingdom) 1993, 14/2 (54-60)
CODEN: TPHSD ISSN: 0165-6147
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Since the discovery of endothelins, peptides with exceptional vasoconstrictor potency that were originally suggested to act by causing the opening of Casup 2sup + channels, it has emerged that these agents are important in intercellular communication in many tissues. They exert their effect through G protein-coupled receptors, of which two classes have been cloned. Robert Miller, John Pelton and John Huggins review the progress made towards a molecular understandinig of ligand recognition by endothelin receptors. Receptor-selective agonists and antagonists have emerged from attempts to understand the three-dimensional structure of the endothelin pharmacophore, from structure-activity studies and from rapid-screening programmes. From the nature of the secretion and action of endothelins, it would seem that these peptides are involved in long-term changes rather than in acute responses to stimuli, and that they are likely to be important in a number of pathological states. Evidence suggests that receptor antagonists with appropriate affinity and selectivity may be useful in the *treatment* of conditions as diverse as hypertension, ulcerogenesis and ciclosporin toxicity.

BRAND NAME/MANUFACTURER NAME: bq 123; fr 901367; fr 139317; pd 142893;
compound 50235
DRUG DESCRIPTORS:

*endothelin receptor; *endothelin--endogenous compound--ec endothelin 1 --drug combination--cb; *endothelin 1--drug interaction--i *endothelin 1 --pharmacology--pd; *endothelin 1 derivative--pharmacology--pd; * endothelin(16-21)--pharmacology--pd; *guanine nucleotide binding protein --endogenous compound--ec
endothelin a receptor; *endothelin b receptor*; receptor subtype; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug development--dv; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug analysis--an; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug combination--cb; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug interaction--it; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl) --pharmacology--pd; cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)--drug comparison--cm; cyclosporin--drug toxicity--to; cyclosporin--pharmacology--pd; 2 ((2 ((2 (((hexahydro 1h azepin 1 yl)carbonyl)amino) 4 methylpentanoyl)amino) 3 (1 methyl 1h indol 3 yl)propionyl)amino) 3 (2 pyridyl)propionic acid--drug analysis--an; 2 ((2 ((2 (((hexahydro 1h azepin 1 yl)carbonyl)amino) 4 methylpentanoyl)amino) 3 (1 methyl 1h indol 3 yl)propionyl)amino) 3 (2 pyridyl)propionic acid--drug development--dv; 2 ((2 ((2 (((hexahydro 1h azepin 1 yl)carbonyl)amino) 4 methylpentanoyl)amino) 3 (1 methyl 1h indol 3 yl)propionyl)amino) 3 (2 pyridyl)propionic acid--drug comparison--cm; 2 ((2 ((2 (((hexahydro 1h azepin 1 yl)carbonyl)amino) 4 methylpentanoyl)amino) 3 (1 methyl 1h indol 3 yl)propionyl)amino) 3 (2 pyridyl)propionic acid--pharmacology--pd; n acetyl 3,3 diphenyl dextro alanylleucylaspartylisoleucylisoleucyltryptophan --pharmacology--pd; n acetyl 3,3 diphenyl dextro alanylleucylaspartylisoleucylisoleucyltryptophan--drug analysis--an; n acetyl 3,3 diphenyl dextro alanylleucylaspartylisoleucylisoleucyltryptophan --drug development--dv; n acetyl 3,3 diphenyl dextro alanylleucylaspartylisoleucylisoleucyltryptophan--drug comparison--cm; unclassified drug
MEDICAL DESCRIPTORS:
*calcium channel; *smooth muscle contraction; *stress
amino acid sequence; animal cell; animal model; animal tissue; cardiovascular disease; central nervous system; heart; human; human cell; human tissue; molecular cloning; nonhuman; priority journal; rat; receptor binding; review; structure activity relation
DRUG TERMS (UNCONTROLLED): compound 50235--drug analysis--an; compound 50235--drug comparison--cm; compound 50235--pharmacology--pd; compound 50235--drug development--dv; fr 901367
CAS REGISTRY NO.: 121377-67-1 (endothelin(16-21)); 136553-81-6 (cyclo(dextro tryptophyl dextro aspartylprolyl dextro valylleucyl)); 79217-60-0 (cyclosporin); 142375-60-8 (2 ((2 ((2 (((hexahydro 1h azepin 1 yl)carbonyl)amino) 4 methylpentanoyl)amino) 3 (1 methyl 1h indol 3 yl)propionyl)amino) 3 (2 pyridyl)propionic acid)
SECTION HEADINGS:
002 Physiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 *Cancer*
018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
032 Psychiatry
048 Gastroenterology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

11/5/5 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

09549409 98257805
LU 302 872 and its racemate (LU 224 332) show balanced endothelin-A/B receptor affinity, high oral activity, and inhibit human prostate tissue contractions.
Raschack M; Gock S; Unger L; Hahn A; Amberg W; Jansen R; Alken P; Weber A ; Hergenroder S

Main Laboratory Ludwigshafen, Germany.
Journal of cardiovascular pharmacology (UNITED STATES) 1998, 31 Suppl 1 pS241-4, ISSN 0160-2446 Journal Code: K78
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9809
Subfile: INDEX MEDICUS

LU 302 872 (racemate LU 224 332) is a new glycerinic acid derivative related to the selective ETA receptor antagonist LU 135 252. LU 302 872 exhibits high and balanced affinity to ETA and ETB receptors (Ki 2.2 and 5.8 nmol/L), whereas LU 135 252 is ETA-selective (Ki 1.4 and 184 nmol/L). Two hours after oral *treatment* of rats with 10 mg/kg of LU 302 872 or of LU 135 252, the big ET-1-induced (20 micrograms/kg i.v.) blood pressure increase is inhibited by 59 +/- 8% or 52 +/- 2% (n = 6-8; p < 0.05 vs. control), whereas bosentan is without effect (-6 +/- 7%; n = 6). In guinea pigs, 10 mg/kg p.o. of LU 302 872 inhibited the big ET-1 (20 micrograms/kg i.v.)-induced bronchospasm (reduction in respiratory volume) by 78 +/- 7% (n = 6; p < 0.05), whereas the ETA antagonist LU 135 252 was ineffective (0.2 +/- 37%; n = 6). Hence, a high oral effectiveness of the new ETA/B antagonist could be demonstrated in two species for both an ETA- or an ETB-mediated response. In human prostate tissue (excised during cystectomy in bladder *cancer* patients), ET-1 and in most cases, the ETB agonist sarafotoxin 6c (S6c) caused contractions of similar magnitude but more sustained than that of norepinephrine (10(-6) mol/L). A high concentration (10(-5) mol/L) of the ETA antagonist LU 135 252 only moderately attenuated ET contractions. The ETA/B antagonist LU 302 872 or its racemate, LU 224 332, dose-dependently inhibited ET-1-induced contractions. S6C dose-response curves, too, were shifted to the right or suppressed by the combined ETA/B antagonist (10(-6) mol/L LU 224 332). LU 302 872 may be a suitable candidate for testing in benign prostate hyperplasia (BPH).

Tags: Animal; Human; In Vitro; Male

Descriptors: *Muscle, Smooth--Drug Effects--DE; *Propionic Acids --Pharmacology--PD; *Prostate--Drug Effects--DE; *Pyrimidines--Pharmacology --PD; *Receptors, Endothelin--Antagonists and Inhibitors--AI; Blood Pressure--Drug Effects--DE; Bronchial Spasm--Physiopathology--PP; CHO Cells ; Endothelins--Antagonists and Inhibitors--AI; Hamsters; Muscle Contraction --Drug Effects--DE; Propionic Acids--Metabolism--ME; Protein Precursors --Antagonists and Inhibitors--AI; Pyrimidines--Metabolism--ME; Rats; Rats, Sprague-Dawley; Receptors, Endothelin--Metabolism--ME; Stereoisomerism

CAS Registry No.: 0 (endothelin A receptor); 0 (endothelin B receptor) ; 0 (Endothelins); 0 (LU 224332); 0 (Propionic Acids); 0 (Protein Precursors); 0 (Pyrimidines); 0 (Receptors, Endothelin); 122462-75-3 (big endothelin)

?ds

Set	Items	Description
S1	1	AU="SCHNEIDER, R. J."
S2	1	AU="JAMALA S"
S3	1	AU="JAMALA S."
S4	3497	ENDOTHELIN B RECEPTOR
S5	74	S4 AND MOLECULE?
S6	0	S5 AND ANTISENSE
S7	31	S5 AND ANTAGONIS?
S8	12	RD (unique items)
S9	81	S4 AND CANCER?
S10	15	S9 AND TREATMENT?
S11	5	RD (unique items)

?s s4 and melanoma

```
          3497  S4
        230872  MELANOMA
    S12   22    S4 AND MELANOMA
?s s12 and inhibit?
Processing
Processed  10 of  14 files ...
Completed processing all files
            22  S12
       4229592  INHIBIT?
```

S13 5 S12 AND INHIBIT?
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S14 2 RD (unique items)
?t s14/5/all

14/5/1 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

01545430 99432261
An endothelin receptor B antagonist *inhibits* growth and induces cell death in human *melanoma* cells in vitro and in vivo.
Lahav R; Heffner G; Patterson PH
Division of Biology, California Institute of Technology, Pasadena, CA 91125, USA.
Proc Natl Acad Sci U S A; 96(20):11496-500 1999 ISSN 0027-8424
Journal Code: PV3
Languages: ENGLISH
Document Type: JOURNAL ARTICLE
Journal Announcement: 199911
Subfile: L; M; X MEDL/99432261
Activation of the endothelin receptor B (ETRB) in cultured melanocyte precursors promotes cell proliferation while *inhibiting* differentiation, two hallmarks of malignant transformation. We therefore tested whether ETRB has a similar role in malignant transformation of *melanoma*. When tested in culture, we find that the selective ETRB antagonist BQ788 can *inhibit* the growth of seven human *melanoma* cell lines, but not a human kidney cell line. This *inhibition* often is associated with increases in pigmentation and in the dendritic shape that is characteristic of mature melanocytes. In three cell lines we also observe a major increase in cell death. In contrast, the endothelin receptor A (ETRA) antagonist BQ123 does not have these effects, although all the cell lines express both ETRA and ETRB mRNA. Extending these studies in vivo, we find that administration of BQ788 significantly slows human *melanoma* tumor growth in nude mice, including a complete growth arrest in half of the mice treated systemically. Histological examination of tumor sections suggests that BQ788 also enhances *melanoma* cell death in vivo. Thus, ETRB *inhibitors* may be beneficial for the treatment of *melanoma*.
Tags: Animal; Human; Support, Non-U.S. Gov't
Major Descriptors: Antineoplastic Agents--Pharmacology--PD; **Melanoma* --Drug Therapy--DT; *Oligopeptides--Pharmacology--PD; *Piperidines --Pharmacology--PD; *Receptors, Endothelin--Antagonists and *Inhibitors* --AI
Minor Descriptors: Cell Division--Drug Effects--DE; Cell Survival--Drug Effects--DE; In Situ Nick-End Labeling; *Melanoma*--Pathology--PA; Mice; Mice, Nude; Receptors, Endothelin--Genetics--GE; Tumor Cells, Cultured
CAS Registry No.: 0 (endothelin B receptor); 0 (Antineoplastic Agents); 0 (BQ 788); 0 (Oligopeptides); 0 (Piperidines); 0 (Receptors, Endothelin)

14/5/2 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

06888871 EMBASE No: 1997173250
Bromodeoxyuridine-induced expression of endothelin(A) in A375 human *melanoma* cells
Ohtani T.; Ninomiya H.; Okazawa M.; Imamura S.; Masaki T.

T. Masaki, Department of Pharmacology, Faculty of Medici Kyoto University, Kyoto 606 [redacted]an
Biochemical and Biophysical Research Communications (BIOCHEM. BIOPHYS. RES. COMMUN.) (United States) 1997, 234/2 (526-530)
CODEN: BBRCA ISSN: 0006-291X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 23

Expression of endothelin (ET) receptor subtypes was examined in an experimental model of A375 human *melanoma* cell differentiation using the pyrimidine analog bromodeoxyuridine (BUdR). BUdR (10 muM)-treated cells had an increased surface area and an increased dendricity, were contact-*inhibited* and lacked tumorigenecity in athymic nude mice. The untreated A375 cells exclusively expressed ET(B) and BUdR-induced phenotypical changes were accompanied by induction of ET(A) expression as evidenced by northern blotting, (sup 1sup 2sup 5I)ET-1 binding assay and (Casup 2sup +)i measurement. Thus, BUdR-induced differentiation of A375 *melanoma* cells may provide a model system to study the receptor subtype switch in melanocyte development.

DRUG DESCRIPTORS:
*broxuridine; *endothelin--endogenous compound--ec
endothelin a receptor--endogenous compound--ec; *endothelin b receptor*
--endogenous compound--ec
MEDICAL DESCRIPTORS:
article; cell differentiation; contact *inhibition*; human; human cell;
melanoma cell; model; northern blotting; priority journal
CAS REGISTRY NO.: 59-14-3 (broxuridine)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry
?ds

Set	Items	Description
S1	1	AU="SCHNEIDER, R. J."
S2	1	AU="JAMALA S"
S3	1	AU="JAMALA S."
S4	3497	ENDOTHELIN B RECEPTOR
S5	74	S4 AND MOLECULE?
S6	0	S5 AND ANTISENSE
S7	31	S5 AND ANTAGONIS?
S8	12	RD (unique items)
S9	81	S4 AND CANCER?
S10	15	S9 AND TREATMENT?
S11	5	RD (unique items)
S12	22	S4 AND MELANOMA
S13	5	S12 AND INHIBIT?
S14	2	RD (unique items)

?s s4 and prostate cancer

	3497	S4
	47921	PROSTATE CANCER
S15	10	S4 AND PROSTATE CANCER

?s s15 and inhibit?

	10	S15
	4229592	INHIBIT?
S16	6	S15 AND INHIBIT?

?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records

S17	2	RD (unique items)

?t s17/5/all

17/5/1 (Item 1 from [redacted]e: 5)
DIALOG(R)File 5:Biosis Previews(R)

10746253 BIOSIS NO.: 199799367398

Methylation of the 5' CpG island of the endothelin B receptor gene is common in human prostate cancer.

AUTHOR: Nelson Joel B(a); Lee Wen-Hsiang; Nguyen Son N; Jarrard David F; Brooks James D; Magnuson Scott R; Opgenorth Terry J; Nelson William G; Bova G Steven

AUTHOR ADDRESS: (a)James Buchanan Brady Urol. Inst., Dep. Urol., A344, Johns Hopkins Bayview Med. Cent., 4940 Easte**USA

JOURNAL: Cancer Research 57 (1):p35-37 1997
ISSN: 0008-5472
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Production of the potent vasoconstrictor endothelin-1 (ET-1) by human prostate cancer cells accompanies prostate cancer progression in vivo. The predominant endothelin receptor expressed by normal prostate epithelium, ET-B, is not expressed by any of the established human prostate cancer cell lines, and ET-B binding is decreased on prostate cancer tissues. ET-B, which may mediate ET-1 clearance and may *inhibit* ET-1 secretion, is encoded by a gene that contains a 5' CpG island encompassing the transcriptional regulatory region. We examined this regulatory region of the ET-B, receptor gene (EDNRB) to determine whether hypermethylation of cytidine nucleotides accompanies decreased ET-B expression in human prostate cancer. We found somatic methylation of CpG island sequences in EDNRB in 5 of 5 human prostate cancer cell lines, 15 of 21 primary prostate cancer tissues, and 8 of 14 prostate cancer metastases (70% of samples overall). Normal tissues contained only unmethylated EDNRB. Treatment of human prostatic carcinoma cell line cultures with 5-azacytidine induced ET-B mRNA expression, suggesting that CpG island methylation changes might accompany the apparent transcriptional silencing of EDNRB in vivo.

DESCRIPTORS:
MAJOR CONCEPTS: Endocrine System (Chemical Coordination and Homeostasis); Genetics; Membranes (Cell Biology); Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics); Neurology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Reproductive System (Reproduction); Urology (Human Medicine, Medical Sciences)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
MISCELLANEOUS TERMS: Research Article; CPG ISLAND SEQUENCE METHYLATION; *ENDOTHELIN B RECEPTOR*; ENDOTHELIN B RECEPTOR GENE; EXPRESSION; NEOPLASTIC DISEASE; *PROSTATE CANCER*; REPRODUCTIVE SYSTEM DISEASE/MALE ; TRANSCRIPTIONAL ACTIVITY; TUMOR BIOLOGY; UROLOGIC DISEASE

CONCEPT CODES:
03508 Genetics and Cytogenetics-Human
10300 Replication, Transcription, Translation
10508 Biophysics-Membrane Phenomena
13012 Metabolism-Proteins, Peptides and Amino Acids
15506 Urinary System and External Secretions-Pathology
16506 Reproductive System-Pathology
17020 Endocrine System-Neuroendocrinology (1972-)
20506 Nervous System-Pathology
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
24006 Neoplasms and Neoplastic Agents-Biochemistry

BIOSYSTEMATIC CODES:
86215 Hominidae

17/5/2 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

06401091 EMBASE No: 1996057579

Endothelin-1 production and decreased endothelin B receptor expression in advanced prostate cancer

Nelson J.B.; Chan-Tack K.; Hedican S.P.; Magnuson S.R.; Opgenorth T.J.; Bova G.S.; Simons J.W.

J. Buchanan Brady Urological Inst., Marburg I, Johns Hopkins Hospital, 600 North Wolfe Street,Baltimore, MD 21287-2411 United States

Cancer Research (CANCER RES.) (United States) 1996, 56/4 (663-668)
CODEN: CNREA ISSN: 0008-5472
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The potent vasoconstrictor endothelin-1 (ET-1) is at its highest concentration in the normal human ejaculate and is associated with the progression of metastatic prostate cancer. ET-1 protein expression is detected in situ in 14 of 14 primary cancers and 14 of 16 metastatic sites of human prostatic carcinoma. Exogenous ET-1 induces prostate cancer proliferation directly and enhances the mitogenic effects of insulin-like growth factor I, insulin-like growth factor II, platelet-derived growth factor, basic fibroblast growth factor, and epidermal growth factor in serum- free conditions in vitro. The ET(A)-selective receptor antagonist A-127722 *inhibits* ET-1-stimulated growth, but the ET(B)-selective receptor antagonist BQ-788 does not. ET-3, an ET(B)-selective agonist, also had no effect on prostate cancer growth. No specific ET(B)-binding sites could be demonstrated in any established human prostate cancer cell line tested, and ET(B) mRNA, detected by reverse transcription PCR, was reduced. The predominance of ET(B) binding on human benign prostatic epithelial tissue is not present in metastatic prostate cancer by autoradiography. In human prostate cancer progression to metastases, ET-1 and ET(A) expression are retained, whereas ET(B) receptor expression is reduced.

DRUG DESCRIPTORS:
**endothelin b receptor*; *endothelin 1--endogenous compound--ec 4 (1,3 benzodioxol 5 yl) 1 (dibutylcarbamoylmethyl) 2 (4 methoxyphenyl) 3 pyrrolidinecarboxylic acid; basic fibroblast growth factor; endothelin a receptor antagonist; epidermal growth factor; n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine; platelet derived growth factor; somatomedin b; somatomedin c
MEDICAL DESCRIPTORS:
**prostate cancer*
apoptosis; article; autoradiography; cancer growth; clinical article; gene expression; human; human cell; human tissue; male; metastasis--complication --co; mitogenesis; priority journal; receptor binding; reverse transcription polymerase chain reaction
CAS REGISTRY NO.: 173864-34-1 (4 (1,3 benzodioxol 5 yl) 1 (dibutylcarbamoylmethyl) 2 (4 methoxyphenyl) 3 pyrrolidinecarboxylic acid); 106096-93-9 (basic fibroblast growth factor); 62229-50-9 (epidermal growth factor); 156161-89-6 (n (2,6 dimethylpiperidinocarbonyl) 4 methylleucyl dextro (1 methoxycarbonyltryptophanyl) dextro norleucine); 63774-77-6, 67763-97-7 (somatomedin b); 67763-96-6 (somatomedin c)
SECTION HEADINGS:
005 General Pathology and Pathological Anatomy
016 Cancer
028 Urology and Nephrology
?ds

Set	Items	Description
S1	1	AU="SCHNEIDER, R. J."
S2	1	AU="JAMALA S"

```
S3          1   AU="JAMALA[redacted]."
S4       3497   ENDOTHELI[redacted] RECEPTOR
S5         74   S4 AND MOLECULE?
S6          0   S5 AND ANTISENSE
S7         31   S5 AND ANTAGONIS?
S8         12   RD (unique items)
S9         81   S4 AND CANCER?
S10        15   S9 AND TREATMENT?
S11         5   RD (unique items)
S12        22   S4 AND MELANOMA
S13         5   S12 AND INHIBIT?
S14         2   RD (unique items)
S15        10   S4 AND PROSTATE CANCER
S16         6   S15 AND INHIBIT?
S17         2   RD (unique items)
?s s4 and ovarian cancer?
            3497  S4
            9072  OVARIAN CANCER?
     S18       0  S4 AND OVARIAN CANCER?
?s s4 and ovarian cancer
            3497  S4
            8450  OVARIAN CANCER
     S19       0  S4 AND OVARIAN CANCER
?s s4 and mammary cancer?
            3497  S4
             432  MAMMARY CANCER?
     S20       0  S4 AND MAMMARY CANCER?
?s s4 and breast cancer?
            3497  S4
          126993  BREAST CANCER?
     S21       0  S4 AND BREAST CANCER?
?s s4 and breast cancer
            3497  S4
          124214  BREAST CANCER
     S22       0  S4 AND BREAST CANCER
?s s4 and breast (s) cancer
            3497  S4
          681133  BREAST
         2651466  CANCER
          393544  BREAST(S)CANCER
     S23       0  S4 AND BREAST (S) CANCER
?
```